Elevated Lipid Levels in Vietnam Veterans with Chronic Posttraumatic Stress Disorder

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Background: *Elevated cholesterol levels have been reported in panic disorder and anger attacks, but not major depression. No data have been reported in posttraumatic stress disorder (PTSD).*

Methods: *Seventy-three male Vietnam veterans with chronic (PTSD) had serum lipid screening upon entry to a 90-day inpatient program.*

Results: *Elevated cholesterol, low-density lipoprotein, triglycerides, and reduced high-density lipoprotein, were frequent in Vietnam veterans with chronic PTSD and are significant risk factors for coronary artery disease.*

Conclusions: *Routine lipid screening may be warranted in this at-risk population. Altered lipid levels may result from activation of the noradrenergic system.* Biol Psychiatry 1999;45:374–377 © *1999 Society of Biological Psychiatry*

Key Words: Posttraumatic stress disorder, lipids, stress, trauma, veterans

Introduction

Elevations in serum cholesterol, a risk factor for coronary artery disease (CAD), have been reported in panic disorder patients (Bajwa et al 1992) and patients with anger attacks (Fava et al 1991), but not in major depression (Hayward et al 1989; Oxenkrug et al 1983; Yates and Wallace 1987). Cholesterol has been reported to be lowered in inmates with aggressive conduct disorder, antisocial personality disorder, and homicidal behavior (Vikkunen and Pentinnen 1979; Vikkunen 1984). Cholesterol and other lipids have not been conclusively demonstrated to be altered in other psychiatric illness, although reports suggest an association of low cholesterol with suicide and violence and possible alterations in schizophrenia (Boston et al 1996).

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As part of a routine admission screening panel administered to patients entering an inpatient posttraumatic stress disorder (PTSD) program, we noted that the majority had elevated serum cholesterol levels (>200 mg/dL). We tested fasting lipid profiles to assess lipid pathology, hypothesizing that serum cholesterol, low-density lipoprotein (LDL), and triglycerides might be elevated in this population. We rechecked the lipid profile in some patients who completed the PTSD program and were maintained on a low-fat diet.

Epidemiologic data on Vietnam veterans (Kulka et al 1990) show no significant elevations in cardiovascular disease or serum lipids; however, these data do not break down Vietnam veterans according to combat exposure or according to level of PTSD symptomatology. Chronic PTSD in Vietnam veterans is associated with significant psychiatric comorbidity as well as biological alterations such as hypersensitive steroid receptors (Yehuda et al, 1991, 1995), changes in thyroid function (Mason et al 1994), and altered catecholamine function (Southwick et al 1995).

Methods and Materials

Seventy-three male Vietnam veterans (mean age = 43.8 ± 3.9 years) suffering from PTSD were consecutively admitted to a 90-day specialized inpatient PTSD unit (SIPU) at the West Los Angeles Veterans Affairs Medical Center. One hundred thirteen male volunteers consecutively admitted to a 21-day inpatient substance abuse program were used as a comparison group. This group was chosen because it matches the PTSD group quite well on demographic factors, including age (no significant difference), ethnicity, and socioeconomic status (SES), as well as controlling for acute hospitalization status and diet. Since the PTSD group had a high rate of lifetime substance abuse, this comorbid condition was also partially controlled for.

Instruments

The Structured Clinical Interview for DSM-III-R (SCID) is a highly reliable, extensively tested clinician-administered interview that gives DSM-III-R diagnoses.

The Vietnam Veteran History Questionnaire (VVHQ) is a highly reliable, self-rated scale that provides premilitary, military, and postmilitary data (Carroll et al 1985).

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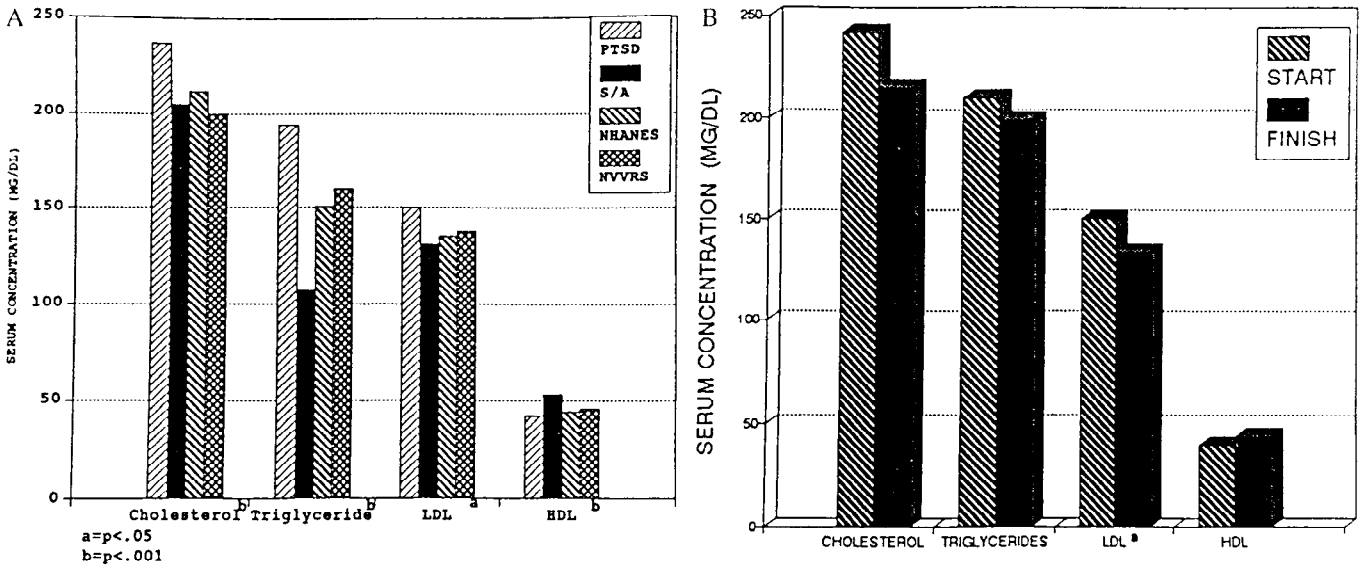

Figure 1. **(A)** Mean serum lipid levels in chronic PTSD veterans (PTSD), Vietnam era veterans (NVVRS), hospitalized substance abusers (S/A), and civilians (NHANES). [a]Significant difference between groups (PTSD and S/A) ($p < .001$). [b]Significant difference between groups (PTSD and S/A) ($p < .05$). **(B)** Lipid levels at start and end of 90-day program. [a]Significant differences between start and end ($p < .05$).

The Los Angeles Symptom checklist (LASC) is a highly reliable, self-rated symptom checklist that includes the DSM-III-R criteria for PTSD as a subset (King et al 1995).

Diagnostic agreement between the SCID and the combination of LASC, VVHQ, and clinical interview was 100% in our first 40 patients. This led us to abandon the SCID as unnecessary for diagnosis in such a homogenous clinical population. In the last 33, diagnosis was made using DSM-III-R criteria on data obtained from two clinical interviews, the VVHQ and the LASC. Patients were accepted to the SIPU only by referral from a mental health clinician who had to certify that the patient had been free of drugs and alcohol for at least 6 months prior to entry. Routine and random drug screening was employed to maintain a drug-free environment. Patients with active psychosis, dementia, schizophrenia, active medical problems, or uncontrollable behavior were excluded. Combat exposure was verified by examination of military discharge papers (DD214) and/or military records. Our program consisted of structured group therapy, psychotropic medications, and individual imaginal exposure therapy (flooding). Most patients received antidepressants or mood stabilizers. Benzodiazepines and antipsychotics were used only rarely. No patients were on lipid-lowering drugs. Fasting lipid profiles were performed in the early morning within 72 hours of admission. A follow-up profile was obtained 3 months later on some patients during the week prior to discharge. Follow-up profiles were not obtained in all patients due to the fact that this procedure was added later in the study. Lipid profiles were determined on a Synchronex CX System (Beckman). Patients with elevated cholesterol (>200 mg/dL) were placed on low-fat diets.

One-way analysis of variance (ANOVA) was employed to compare the PTSD group and the substance abuse group. Two-tailed t tests were used to compare the beginning and final [illegible] levels of the PTSD group. Chi square analysis was performed to compare the percentages of patients with cholesterol above a certain level.

Results

PTSD veterans had a serum cholesterol of 237 ± 64 (mean ± SD) mg/dL, a triglyceride level of 194 ± 129 mg/dL, a LDL cholesterol level of 151 ± 45 mg/dL, and a high-density lipoprotein (HDL) cholesterol level of 42 ± 13 mg/dL (Figure 1). In the PTSD group, mean cholesterol was substantially higher than in Vietnam veterans overall (200 mg/dL, Kulka et al 1990), the general male population of comparable age (212 mg/dL, Johnson et al 1993), and a comparison group of veterans admitted for substance abuse (SA) (205 mg/dL, $F = 14.54$, df = 1,189, $p < .0002$). Mean PTSD triglyceride and LDL levels were also elevated compared to these three groups (Figure 1A) ($F = 39.5$, df = 1,185, $p < .0001$; $F = 8.14$, df = 1,181 $p = .0048$ compared to the SA group). Mean PTSD HDL levels (higher levels protect against coronary artery disease) were less than all three comparison groups and below the recommended level of 45 mg/dL.

More than 70% of patients had cholesterol levels greater than 200 mg/dL, with a range of 147–581 mg/dL. Thirty-eight percent had cholesterol levels greater than 240 mg/dL [defined as moderate risk for coronary artery disease by the National Consensus Panel (1985)], and 28% had cholesterol levels greater than 260 mg/dL (high risk). In the general male population of this age, 23% have cholesterol levels greater than 240 mg/dL and 10% have

cholesterol levels greater than 260 mg/dL (Johnson et al 1993).

There was no significant difference in mean lipid levels between PTSD patients with (243 mg/dL) and without (258 mg/dL) current major depression ($p = .65$). Other comorbid conditions (bipolar disorder, panic disorder, antisocial personality disorder) were far less frequent (<10%).

After 90 days in the SIPU on a low-fat diet, LDL levels decreased significantly from 154 ± 42 to 133 ± 40 mg/dL, ($t = 2.54$, df = 11, $p < .05$). Cholesterol and triglyceride levels declined while HDL levels increased, but these changes did not reach significance (Figure 1B).

In the SA group, triglyceride levels were substantially lower than in veteran and civilian groups, and HDL levels were somewhat higher.

Discussion

Our results, though suggestive, should be interpreted with caution. Although patients were certified alcohol- and drug-free by the referring clinicians, violations of sobriety are often difficult to detect, and over 80% of this population has a lifetime history of drug and alcohol abuse (most within the past year). Alcohol can raise triglyceride levels significantly, although some studies suggest a mixed effect of alcohol on cholesterol level, with little effect at moderate consumption levels, and a decrease of LDL at high consumption levels (Castelli et al 1977). Comorbidity of major depression was also significant (~50%), but at least three studies suggest that cholesterol is not elevated in major depression (Bajwa et al 1992; Oxenkrug et al 1983; Yates and Wallace 1987). The acute stress of hospitalization may also have elevated lipid levels, but our SA group was also acutely hospitalized. Hospitalization might have reflected acute stress in the patients' lives; however, the usual wait to enter the program was 6–8 weeks, making severe acute stress unlikely.

Our comparison groups are also imperfect since the Vietnam veteran data are several years old and cholesterol rises with age in this age group; however, even after correcting for the rise due to age (~8–10 mg/dL), the PTSD group was still substantially elevated. The National Vietnam Veterans readjustment study is a comprehensive database on veterans from the period 1988–1989. The cholesterol data are from all Vietnam veterans whether assigned to combat or not. Since a significant minority of these veterans had or have PTSD, using this group probably lessens the likelihood of finding differences due to PTSD.

The general male civilian population is not a perfect comparison group for PTSD veterans. The National Health and Nutrition Examination Survey (NHANES) was conducted in 1988–1991 on 7775 participants age 20 years and older. This survey of the general adult population of the U.S. shows a substantial decline in cholesterol levels from earlier data (1976–1980) (Johnson et al 1993). This suggests that our current data may underestimate the difference between PTSD patients and the general population.

The substance abuse group is well matched on demographic variables, but the influence of very recent substance use on lipid levels is unknown. Our present results suggest that recent substance abuse may result in lowered triglycerides (perhaps due to lowered dietary intake) and increased HDL (perhaps due to alcohol consumption).

The causes of these lipid alterations are uncertain. Unfortunately we know little about the prehospital dietary intake of these patients. Bajwa et al (1992) have suggested increased noradrenergic activity in panic disorder as a possible mediator of increased cholesterol. Plasma catecholamines have also been associated with higher serum cholesterol in a large group of hypertensive patients (Kjeldsen et al 1992). Increased catecholamine levels have been documented in a similar population of PTSD veterans, and may account for the lipid alterations reported here (Southwick et al 1995). Comparisons between panic disorder and PTSD have been suggested, and an increase in noradrenergic activity has been hypothesized in PTSD (Krystal et al 1989). Increased physiologic reactivity (heart rate, blood pressure) in PTSD is well documented, and these measures correlate positively with cholesterol level in hypertensive men (Kjeldsen et al 1992).

Our follow-up results suggest that lipid levels, especially LDL, may tend to normalize during inpatient treatment. While these results may simply reflect regression toward the mean, the effects of dietary modification and traumatic stress reduction may also be important. Further studies utilizing outpatient baseline monitoring are needed to address these issues.

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